REMARKS

Status of the Claims

Claims 1-40 are pending. Claims 3, 17-31 and 37-40 have been withdrawn from consideration and claims 1, 2, 4-16 and 32-36 are under active examination. Claim 36 was objected to as being dependent on a base claim but would be allowable if rewritten in independent form.

Information Disclosure Statement

As noted above, an IDS also accompanies the filing of this Submission under 37 C.F.R. § 1.114. Consideration of the references is requested.

35 U.S.C. § 103(a)

A. Claims 1, 2, 4-10 and 13-16

Claims 1, 2, 4-10 and 13-16 were again rejected as allegedly obvious over Vajdy in view of Keefer et al. (Final Office Action, paragraph 2). Vajdy was cited for teaching intranasal administration of mice with HIV and an LTK63 adjuvant. *Id.* Keefer was cited for teaching particular concentrations of gp120. *Id.* The rejection was premised on the assertion that, pursuant to MPEP § 2144.05, Applicants are required to show that the particular claimed range is "critical." In addition, it was asserted that applicants are entitled to claim only the concentration shown in the Examples – in the instant case 300 μg (claim 35). *Id.*

As noted by the Examiner, claims 1, 2, 4-10 and 13-16 require specific amounts of an HIV Env antigen be used in combination with an LTK63 adjuvant. Vajdy's Abstract does not disclose any amounts whatsoever of HIV Env antigen and does not teach that the presence of LTK63 enhances the immune response generated against HIV Env antigens (Vajdy, lines 5-8):

> To induce anti-envelope Abs we compared intra-nasal immmunizations of mice with soluble gp120 with soluble oligomeric (O)gp140 in the presence of absence of a genetically detoxified mutant of the E. Coli LT toxin, LTK63. We found that Ogp140 combined with LTK63 induced serum Ab responses specific for both Ogp140and monomeric gp120.

This Abstract does not teach whether LTK63 enhanced the Ab response as compared to administration of Ogp140 alone and, again, fails to teach any specific amounts of Env antigens.

Furthermore, Vajdy is entirely focused on dual administration of HIV Env and Gag antigens (or VLPs) in order to induce "both cell mediated and humoral responses against HIV gag and envelope proteins." (Vajdy, last two lines). Therefore, Vajdy not only contains no teachings regarding Env antigen concentrations, this Abstract teaches away from using Env antigens alone.

Keefer fails to supplement Vajdy's Abstract. This reference does not teach anything about compositions comprising HIV Env and LTK63. The Examiner does not in any indicate that the cited Keefer reference discloses anything about HIV Env antigen concentrations when used with the LTK63 adjuvant.

Moreover, whereas the instant application clearly teaches that administration of combination HIV Env and LTK63 compositions results in raised serum titers in all experimental animals (Table 2 on page 25), Vajdy is silent in this regard and Keefer teaches that 160 μg doses of HIV Env antigens (without LTK63) resulted in, at best, 16 out of 20 animals exhibiting positive EIA employing antigen scores. (See, Table 3, Keefer).

Accordingly, Applicants have shown that combining HIV Env antigens with LTK63 is critical to producing an immune response, and by so doing have rebutted the obviousness rejection (see, M.P.E.P. § 2144.05 III).

Applicants further note that the assertion that they are entitled to claim only that which is exemplified is untenable. (Final Office Action, paragraph 2). It is axiomatic that multiple working examples are not required. Indeed, the examples provided herein clearly demonstrate that combining HIV Env antigens with LTK63 provides superior results to HIV Env antigen administration alone. Accordingly, assuming, for the sake of argument only, that a *prima facie* case of obviousness was made out, it has been rebutted. Thus, the rejection cannot be sustained.

B. Claims 1, 11 and 12

Claims 1, 11 and 12 were rejected as allegedly obvious over Vajdy in view of Keefer as applied to claims 1, 2, 4-10 and 13-16 above and in further view of Kumar and Narayan, Haynes, Kang, Tobery and Siliciano, Cease and Berzofsky and Vogel. (Final Office Action, paragraph 3). It was acknowledged that Vajdy and Keefer do not teach compositions comprising HIV regulatory proteins (*e.g.*, Tat and Rev) and/or HIV accessory proteins (*e.g.*, Vpu, Vpr, Vif, and Nef) as set forth in claims 11 and 12. *Id.* However, the Examiner again maintained that the

motivation to combine derives from the suggestion in the prior art to "broaden the scope of the immune response." *Id.*

Applicants submit that the Office has not established that the art as a whole contains the suggestion to "broaden the scope of the immune response" by combining HIV Env antigens with LTK63 in the amounts claimed. Claims 1, 11 and 12 are not directed to methods of eliciting immune responses or even to methods of "broadening" immune responses to HIV Env. Rather, these claims are directed to compositions comprising LTK63, specific amounts of an HIV Env antigen and, for claims 11 and 12, further comprising an HIV regulatory or accessory protein. Such compositions are not taught or suggested by the references and the alleged motivation to combine is improperly based on a particular intended use to broaden an immune response. Indeed, even if the claims did require that an immune response be elicited, the "broadness" of the response cannot be the basis for an obviousness rejection, as it would be amply clear to the skilled artisan that HIV Env antigens alone elicit such immune responses and nowhere do the references teach that LTK63 "broadens" the immune response.

B. Claims 32-35

Claims 32-35 were also rejected as allegedly obvious over Vajdy and Keefer as applied to claims 1, 2, 4-10 and 13-16 above and in further view of Kumar and Narayan. (Final Office Action, paragraph 4). It was acknowledged that Vajdy does not teach particular amounts of HIV Env antigen set forth in the claims. With regard to Keefer, no indication is given that this references teaches ogp140 or KTK63. *Id.* Kumar and Narayan were cited for teaching the use of live attenuated retroviral vaccines comprising gp120 at a concentration of 100 and 50 μg per inoculation. *Id.* It was alleged that the motivation to combine Vajdy and Keefer with the various secondary is that the "resultant vaccine would be more broadly based" and that there was a reasonable expectation of success. *Id.* at page 5.

Claims 32 to 35 are directed to compositions comprising between 100 and 300 μg of an HIV Env antigen in combination with an LTK63 adjuvant. As noted above with regard to claims 1, 2, 4-10 and 13-16, Vajdy does not disclose any amounts whatsoever of HIV Env antigen and teaches away from using HIV Env antigens alone. Keefer does not disclose anything about HIV Env antigen concentrations when used with the LTK63 adjuvant. Moreover, as detailed above,

Keefer teaches away from using dosages lower than 640 μg of HIV Env antigen. On this basis alone, there is no motivation to combine the references to arrive at the subject matter of claims 32-35 and the rejection should be withdrawn.

In addition, claim 35 specifies that the HIV Env antigen is an ogp140 (wild-type). There is nothing in Keefer, Kumar or Narayan regarding ogp140, including particular concentrations of this antigen. Therefore, again, there is no motivation to combine these references as set forth and, in fact, there is no combination of these references that would result in the particularly claimed subject matter. Accordingly, Applicants respectfully request that the rejections be withdrawn.

CONCLUSION

In light of the above remarks and amendments, Applicants submit that the present application is in condition for allowance. Early notice to that effect is earnestly solicited.

If the Examiner contemplates another action, or if a telephone conference would expedite allowance of the claims, the Examiner is invited to contact the undersigned.

The Commissioner is hereby authorized to charge any fees and credit any overpayment of fees which may be required under 37 C.F.R. §1.16, §1.17, or §1.21, to Deposit Account No. 18-1648.

Please direct all further written communications regarding this application to:

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Respectfully submitted,

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